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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,056	12/11/2000	Leonard Katz	4952.US.C1	4609

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EXAMINER

MOORE, WILLIAM W

ART UNIT PAPER NUMBER

1652

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,056

Applicant(s)

KATZ ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59, 61, 72-75, 79-81 and 84 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59, 61, 72-75, 79-81 and 84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Response to Amendment

Applicant's Amendment After Final filed 11 February 2005, deleting claim 77 and amending claims 81 and 84, overcomes the rejections of record of claims herein under the first and second paragraphs of 35 U.S.C. § 112, first and second paragraphs. This communication reopens prosecution on the merits, however, on the issue of the scope of enablement of methods of claims 59, 61, 79-81 and 84, may be practiced, thus is not made final. While the term of a patent issuing on this application over the term of U.S. Patent No. 5,824,513 was disclaimed in a Terminal Disclaimer filed 27 September 2004, a further Terminal Disclaimer will overcome a new rejection under the judicially created doctrine of obviousness-type double patenting made below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 59, 61, 72-75, 79-81 and 84 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,004,787. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of the pending claims 59, 61, 72-75, 89-81 and 84 herein is also a method of the patented claim which, on the basis

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of the patent disclosure, permits the modification of the biosynthesis of a macrolide polyketide to produce a specifically altered polyketide analog by adding or disrupting the coding regions within a polyketide synthase gene that specify, *inter alia*, any of the β -ketoreductase, dehydratase and enoylreductase activities.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 60, 72-75, 89-81 and 84 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of biosynthesis of modified polyketides by genetic manipulation of polyketide synthase-encoding DNA sequences endogenous to a transformed host cell wherein the polyketide is produced, does not reasonably provide enablement for methods of biosynthesis of modified polyketides by host cells wherein polyketide synthase-encoding DNA sequences are heterologous to a transformed host cell that does not produce the same or a related polyketide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

It is agreed that the specification, in view of the prior art of record herein, enables alteration of DNA sequences of genes encoding generic polyketide synthases according to a claimed method and the subsequent, productive, transformation of host cells other than the cell that is the source of the gene encoding the polyketide synthase before its alteration, by placing the altered polyketide synthase-encoding DNA sequence in a context for expression by a heterologous host cell. Yet neither the specification nor the prior art of record herein teach how a generic, heterologous, host cell may survive the practice of a claimed method after transformation. Claims 59, 60, 72-75, 89-81 are subject to this rejection because all embrace methods of producing modified polyketides by transforming of any kind of host cell with a modified DNA sequence that encodes a modified polyketide synthase, whether or not the transformed host itself produced a

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polyketide prior to transformation and whether or not the transformed host cell was resistant to the toxicity of the same or similar polyketide prior to transformation.

This rejection is not directed to the transformation of a host cell with polyketide synthase-encoding nucleic acid altered according to a claimed method wherein the altered polyketide synthase-encoding nucleic acid is not in a context for expression by that cell. It is, rather, directed to practice of a method wherein a host cell is transformed with an altered polyketide synthase-encoding nucleic acid in a context for expression by the transformed cell and that cell is susceptible to the toxicity of the modified polyketide produced in the cell upon recombinant expression of the modified polyketide synthase. Both the prior art of record herein and the instant specification, see, e.g., page 1 line 35, teach that many polyketides are toxic compounds - either anti-microbial or anti-fungal - for unicellular organisms. There is no suggestion or teaching in the specification of how to protect a prospective host cell from the toxic effects of a modified polyketide produced after transformation of the host cell according to a claimed method when the polyketide produced is unrelated structurally to a polyketide the host cell itself produces, or if the host cell itself produced no polyketide. It is well settled that the first paragraph of 35 U.S.C. § 112 requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing eight factors relevant to analysis of enablement). Applying the analysis discussed in *Wands* to Applicant's disclosure, it is apparent that:

- the specification lacks adequate, specific, guidance for practicing a claimed method with transformed host cells susceptible to the toxic effects of a modified polyketide to be prepared according to the method,
- the specification lacks working examples wherein a cell susceptible to the toxic effects of a modified polyketide to be prepared according to the method is

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transformed with a modified, heterologous, polyketide synthase-encoding DNA sequence and survives the production of the modified polyketide, in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support the practice a claimed method with transformed host cells susceptible to the toxic effects of a modified polyketide to be prepared according to the method, and, unpredictability exists in the art where no cells other than those of genera of the order *Actinomycetales* are demonstrated to have some resistance to the toxic effects of some, but not all, polyketides produced by species of other genera in that order.


Thus the scope of methods practiced with transformed microorganisms embraced by the statement, "a polyketide-producing microorganism", in the preamble of claim 84 is unsupported by the present specification even if taken in combination with teachings available in the prior art. Amending the preamble and clause (4) of claim 84 to require genetic manipulation of a polyketide-producing *Actinomycetales* cell and transformation of an *Actinomycetales* host cell will overcome this rejection.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone number for all communications for the organization where this application or proceeding is assigned is now 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
8 March 2005



PONNATHAPU ACHUTAMURTHY
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